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REMARKS

Claims 1-49 were pending in the subject application. Applicant herein above has amended claim 1, 8, 11, 15, 20 and 49 and canceled claims 17 and 26-48. Accordingly, claims 1-16, 18-25 and 49 are presented for the Examiner's consideration. Support for the amendments of claims 1, 8 and 49 may be found inter alia in the subject specification on page 33, lines 12 to 20, support for the amendment of claim 11 may be found inter alia in the subject specification from page 18, line 24 to page 19, line 2 and support for the amendments of claims 15 and 20 may be found inter alia in the subject specification on page 13, lines 10 to 20.

Claims Objections

In the January 3, 2002 Office Action, the Examiner objected to claim 11 because claim 11 depends from two different claims that are not referred to in the alternative. The Applicant has modified claim 11 to be dependent on only one claim. Support for the amendment of claim 11 may be found inter alia in the subject specification from page 18, line 24 to page 19, line 2.

Rejection under 35 U.S.C. § 112, first paragraph

On page 2 of the January 3, 2002 Office Action, the Examiner rejected claims 1, 3-15, 17-25, and 49 under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The Examiner alleged that the Applicant's claims are directed to a nucleotide sequence comprising a human ABC1 promoter as set forth in SEQ ID NO: 1, nucleotide sequences that hybridize to the

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same promoter, a nucleotide sequence that is functionally equivalent to the same promoter as well as host cells comprising a recombinant expression construct that comprises the same nucleotide sequences in operable linkage with a selected coding sequence. The Examiner also alleged that the Applicant's claims are directed to methods of expressing foreign DNA in a host using a vector comprising the same nucleotide sequences. The Examiner rejected the claims directed to nucleotide sequences that are functionally equivalent to the sequence set forth in SEQ ID NO: 1 and nucleotide sequences that hybridize to the sequence set forth in SEQ ID NO: 1. The Examiner alleged that the specification fails to describe any variants of the nucleotide sequence of SEQ ID NO: 1 that can direct expression of heterologous nucleotide sequences in a host cell.

In response, without conceding the correctness of the Examiner's position but solely to advance the prosecution of the subject application, the Applicant has amended claims 1 and 49 and canceled claim 17, eliminating the functional language from the claims and substituting for it, language defining the specific nucleotide sequence segments.

The Applicant disagrees with the Examiner's application of Fiddes v. Baird, 30 USPQ2d 1481 (1985) and Amgen v. Chugai, 18 USPQ2d 1016 (Fed. Cir. 1991). These cases discuss DNA sequences that code for amino acid sequences. The subject application is for a promoter sequence, not a DNA sequence that codes for an amino acid sequence. Notwithstanding the above argument, the Applicant has, as mentioned previously, amended claims 1 and 49 to recite a promoter comprising a nucleotide sequence containing the segment of SEQ ID NO: 1 located between -469 bp and +101 bp. The Applicant discloses in the specification on page 33 lines 12-20 that this region of SEQ ID NO: 1 contains the nucleotides that

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are responsible for up-regulation presumably as binding sites for LXR $\alpha$ , LXR $\beta$  and RXR. The binding of LXR $\alpha$ , LXR $\beta$  and RXR activates the human ABC-1 promoter.

The Applicant is claiming homologs of SEQ ID NO:1 which are structurally similar to SEQ ID NO:1. The Applicant discloses, in the specification on page 16, line 33 to page 17, line 9 as well as in the reference cited therein, that one skilled in the art would be able to use Southern hybridization under stringent conditions to produce DNA sequences that are 95% homologous with SEQ ID NO:1. One skilled in the relevant art would be aware that the claimed promoter's activity comes from molecular interaction and that all such activity would not be eliminated merely by small changes in the nucleotide sequences of the promoter. Indeed, claims for promoters with language claiming sequences that have been hybridized under stringent conditions have been allowed by the U.S. Patent and Trademark Office in the past( e.g., US 6,392,030 B1). Therefore, the number of homologs of SEQ ID NO:1 that retain the same activity as SEQ ID NO:1 is rather small.

Applicant respectfully submit that the claims, as amended, meet the written description requirement of 35 U.S.C. 112 and therefore, the applicant should not be limited solely to SEQ ID NO:1. in claims 1 and 49.

Claims 3-15, and 17-25 all depend directly or indirectly on claim 1. As a result, these claims also include what is recited in claim 1, i.e., a promoter of SEQ ID NO:1, a promoter containing the specified subsection of SEQ ID NO:1 and promoters of hybridized sequences of both. Therefore, these claims also meet the written description requirement of 35 U.S.C. 112.

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In light of the amendment to claims 1 and 49 and applicant's comments regarding the same, applicant requests that the Examiner reconsider and withdraw his rejection of claims 1, 3-15, 17-25, and 49.

The Examiner rejected claims 10-13 and 15-25 under 35 U.S.C. § 112, first paragraph, alleging the specification, while being enabling for a host cell transformed *in vitro* with a recombinant expression construct comprising the nucleotide sequence set forth in SEQ ID NO: 1 operably linked to a foreign nucleotide sequence encoding a polypeptide of interest and an *in vitro* method of expressing foreign DNA in a host cell using the same recombinant expression construct, does not reasonably provide enablement for a host cell transformed *in vitro* with a recombinant expression construct comprising variants of the nucleotide sequence set forth in SEQ ID NO: 1 operably linked to a foreign nucleotide sequence encoding a polypeptide of interest and an *in vitro* method of expressing foreign DNA in a host cell using the same recombinant expression construct or a host cell transformed *in vivo* with any expression construct and an *in vivo* method of expressing foreign DNA in a host cell.

In response, the Applicant notes that "A patent need not teach, and preferably omits, what is well known in the art." Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1986). Methods for preparing recombinant expression constructs and expressing them *in ex vivo* and *in vivo* were well known to one skilled in the relevant art at the time of filing of the subject application. The removal of cells, introduction of a gene transfer vector and reinsertion of cells, (that is *ex vivo*), was disclosed *inter alia* by Kashani-Sabet et al (*Cancer Research* 54: 900-902, 1994) and Yamazaki et al (*Journal of the*

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National Cancer Institute 90: 581-587, 1998). In vivo techniques of introduction were also well known by the time of the filing of the subject application and were disclosed *inter alia* by Bellon et al (*Hum. Gene Ther.* 8(1) 15-25, 1997) and by Cao et al (*In Vivo* 13(2) 181-187, 1999).

Therefore, the Applicant's claims 10-13 and 15-25 meet the requirements of 35 U.S.C. § 112, first paragraph. Applicant requests that the Examiner reconsider and withdraw the rejection of claims 10-13 and 15-25.

**Rejection under 35 U.S.C. § 112, second paragraph**

On page 8 of the January 3, 2002 Office Action, the Examiner rejected claims 1-25 and 49 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleged that claims 1 and 8 are indefinite as written, and the term "capable of" renders the claim indefinite because it is unclear if the human ABC promoter can actually direct transcription of a heterologous coding sequence.

In response, the Applicant has amended claims 1, 8 and 49 to clarify Applicant's invention without conceding the correctness of the Examiner's position but solely to advance prosecution of the subject application.

On page 9 of the January 3, 2002 Office Action, the Examiner rejected claim 49 as being indefinite as written. The Examiner alleged that claim 49 recites an isolated human ABC 1 gene comprising six exons and a promoter. The Examiner further alleged that the specification described the ABC 1 gene to span a minimum

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of 70KB and to contain at least 49 exons and is therefore inconsistent with Claim 49.

In response, the Applicant has amended claim 49 to clarify Applicant's invention without conceding the correctness of the Examiner's position but solely to advance prosecution of the subject application.

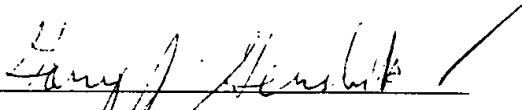
In view of the above mentioned amendments and remarks, the Applicant requests that the Examiner reconsider and withdraw the rejections set forth in the January 3, 2001 Office Action.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorney invites the Examiner to telephone him at the number provided below.

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No fee, other than the enclosed \$460.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents,  
Washington, D.C. 20231.

*Gary J. Gershik 7/3/00*

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**Attachment A**  
**(Marked-up Claims to show amendments)**

1. (Amended) An isolated human *ABC1* promoter that capable of ~~directing~~ transcription of a heterologous coding sequence positioned downstream therefrom, wherein the promoter is selected from the group consisting of:
  - (a) a promoter comprising nucleotides having the nucleotide sequence shown in SEQ ID NO: 1 ;
  - (b) a promoter comprising a nucleotides having ~~the nucleotide sequence functionally equivalent to the nucleotide sequence shown in beginning at bp -469 and ending at bp +101 of~~ SEQ ID NO: 1; and
  - (c) a promoter comprising a nucleotides having ~~the nucleotide sequence that hybridizes to~~ a sequence complementary to the promoter of (a) or (b) in a Southern hybridization reaction performed under stringent conditions.
2. The promoter of claim 1, wherein the promoter comprises the nucleotide sequence shown in SEQ ID NO: 1.
3. The promoter of claim 1, wherein the promoter comprises a nucleotide sequence that is at least 87% homologous to SEQ ID NO: 1.
4. The promoter of claim 3, wherein the promoter comprises a nucleotide sequence that is at least 95% homologous to SEQ ID NO: 1.
5. A recombinant expression construct effective in directing the transcription of a selected coding sequence which comprises:
  - (a) a human *ABC1* promoter nucleotide sequence according to claim 1; and
  - (b) a coding sequence operably linked to the promoter, whereby the coding sequence can be transcribed and translated in a host cell, and the promoter is heterologous to the coding sequence.

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6. The recombinant expression construct of claim 5, wherein the coding sequence encodes a transporter polypeptide.
7. The recombinant expression construct of claim 6, wherein the transported polypeptide is ABCA1 transmembrane transporter protein.
8. (Amended) The recombinant expression construct of claim 6, further comprising a nucleic acid segment encoding a transactivator protein that capable of upregulatesing the ABC1 promoter.
9. The recombinant expression construct of claim 8, wherein the transactivator protein is the Liver-X-Receptor, the Retinoid-X-Receptor, or a heterodimer of the Liver-X-Receptor and the Retinoid-X-Receptor.
10. A host cell comprising the recombinant expression construct of claim 5.
11. (Amended) The host cell of claim 10, wherein the host cell is stably transformed with the recombinant expression construct of claim 5.
12. The host cell of claim 10, wherein the host cell is a macrophage.
13. The host cell of claim 10, wherein the host cell is an immortalized cell.
14. The host cell of claim 10, wherein the cell is selected from the group consisting of RAW cells, African green monkey CV-1 cells and human 293 cells.
15. (Amended) A method for expressing a foreign DNA in a host cell comprising: introducing into the host cell a gene transfer vector comprising ~~an~~ the ABC1 promoter according to claim 1 operably linked to a the foreign DNA encoding a desired polypeptide or RNA, wherein said foreign DNA is expressed.
16. The method of claim 15; wherein the promoter nucleotide sequence is identical to the sequence represented by SEQ ID NO: 1.
17. ~~The method of claim 15, wherein the promoter nucleotide sequence is a nucleotide sequence functionally equivalent to the ABC1 promoter sequence represented in SEQ ID NO: 1.~~

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18. The method of claim 15, wherein the gene transfer vector encodes and expresses a reporter molecule.
19. The method of claim 18, wherein the reporter molecule is selected from the group consisting of beta-galactosidase, beta-glucuronidase, luciferase, chloramphenicol acetyltransferase, neomycin phosphotransferase, and guanine xanthine phosphoribosyltransferase.
20. (Amended) The method of claim 15, wherein the introducing is carried out by ~~a means selected from the group consisting of~~ adenovirus infection, liposome-mediated transfer, topical application to the cell, and or microinjection.
21. The method of claim 15, further comprising introducing into the cell a gene transfer vector comprising a nucleic acid segment encoding a transactivator protein capable of upregulating the ABC1 promoter.
22. The method of claim 21, wherein the transactivator protein is the Liver-X-Receptor, the Retinoid-X-Receptor, or a heterodimer of the Liver-X-Receptor and the Retinoid-X-Receptor.
23. The method of claim 15, further comprising contacting the cell with a transactivator protein capable of upregulating the ABC1 promoter.
24. The method of claim 23, wherein the transactivator protein is the Liver-X-Receptor, the Retinoid-X-Receptor, or a heterodimer of the Liver-X-Receptor and the Retinoid-X-Receptor.
25. The method of claim 24, further comprising contacting the cell with an agonist of the Liver-X-Receptor, of the Retinoid-X-Receptor, or of a heterodimer of the Liver-X-Receptor and the Retinoid-X-Receptor.
26. ~~A method of determining whether a chemical not previously known to be a modulator of the human ABC1 gene transcriptionally modulates the expression of the human ABC1 gene which comprises:~~  
~~(a) contacting a sample which contains a predefined number of identical eucaryotic cells with a predetermined concentration of the chemical to be tested, each cell comprising a DNA construct consisting essentially of in 5' to 3' order,~~

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(i) a modulatable transcriptional regulatory sequence of the ABC1 gene,  
(ii) the ABC1 promoter of claim 1, and  
(iii) a reporter gene which expresses a polypeptide that produces a detectable signal, coupled to, and under the control of, the ABC1 promoter, under conditions wherein the chemical if capable of acting as a transcriptional modulator of the ABC1 gene, causes a detectable signal to be produced by the polypeptide expressed by the reporter gene;

(b) quantitatively determining the amount of the signal produced in (a); and

(c) comparing the amount of signal determined in (b) with the amount of signal produced and detected in the absence of any chemical being tested or with the amount of signal produced and detected upon contacting the sample in (a) with other chemicals, thereby identifying the test chemical as a chemical which causes a change in the amount of detectable signal produced by the polypeptide expressed by the reporter gene, and determining whether the test chemical specifically transcriptionally modulates expression of the human ABC1 gene.

27. The method of claim 26, wherein each cell expresses a transactivator protein capable of upregulating the ABC1 promoter.
28. The method of claim 27, wherein the transactivator protein is the Liver X Receptor, the Retinoid X Receptor, or a heterodimer of the Liver X Receptor and the Retinoid X Receptor.
29. The method of claim 26, further comprising contacting the cells with a transactivator protein capable of upregulating the ABC1 promoter.
30. The method of claim 29, wherein the transactivator protein is the Liver X Receptor, the Retinoid X Receptor, or a heterodimer of the Liver X Receptor and the Retinoid X Receptor.
31. The method of claim 26, wherein the sample comprises identical cells in monolayers.
32. The method of claim 26, wherein the sample comprises identical cells in suspension.

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33. The method of claim 26, wherein the identical cells comprise human, animal, or plant cells.
34. The method of claim 26, wherein the predefined number of identical cells is from about 1 to about  $5 \times 10^5$  cells.
35. The method of claim 26, wherein the predetermined concentration is from about 1.0 pM to about 20 mM.
36. The method of claim 26, wherein the predetermined concentration is from about 10 nM to about 500 mM.
37. The method of claim 26, wherein the contacting is effected from about 1 hour to about 24 hours.
38. The method of claim 26, wherein the contacting is effected with more than one predetermined concentration of the molecule to be tested.
39. The method of claim 26, wherein the modulatable transcriptional regulatory sequence comprises a cloned genomic regulatory sequence.
40. The method of claim 26, wherein the DNA construct consists essentially of more than one modulatable transcriptional regulatory sequence.
41. The method of claim 26, wherein the reporter gene is inserted downstream of the ABC1 promoter by homologous recombination.
42. The method of claim 26, wherein the reporter gene encodes a luciferase, chloramphenicol acetyltransferase, beta-glucuronidase, beta-galactosidase, neomycin phosphotransferase, or guanine xanthine phosphoribosyltransferase.
43. The method of claim 26, wherein the reporter gene is the ABC1 gene.
44. A method of treating atherosclerosis in a subject which comprises administering to the subject a therapeutically effective amount of a chemical selected by the method of claim 26 to modulate expression of the human ABC1 gene.
45. A method of simultaneously screening a plurality of test chemicals to determine whether the chemicals are capable of transcriptionally modulating the ABC1 gene which comprises

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~~simultaneously screening the test chemicals against each of the genes of interest according to the method of claim 26.~~

46. ~~A transgenic non-human mammal whose germ or somatic cells contain the promoter of claim 1 introduced into the mammal, or an ancestor thereof, at an embryonic stage.~~
47. ~~The transgenic non-human mammal of claim 46, wherein the mammal is a mouse.~~
48. ~~A compound which modulates expression of the human ABC1 gene, which has been identified by the method of claim 26.~~
49. (Amended) An isolated human ABC1 gene comprising at least six exons and a promoter, wherein the promoter is selected from the group consisting of:
  - (a) a promoter comprising nucleotides having the nucleotide sequence shown in SEQ ID NO: 1 ;
  - (b) a promoter comprising a nucleotides having the nucleotide sequence functionally equivalent to the nucleotide sequence shown in beginning at bp -469 and ending at bp +101 of SEQ ID NO: 1; and
  - (c) a promoter comprising a nucleotides having the nucleotide sequence that hybridizes to a sequence complementary to the promoter of (a) or (b) in a Southern hybridization reaction performed under stringent conditions.